SELECTED TOPICS IN LABORATORY ANIMAL MEDICINE. VOLUME XXII. THE GUINEA PIG

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This review discussed all pertinent aspects of the use, care, and management of the guinea pig, Cavia porcellus, in the biomedical research environment.

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NOTICES

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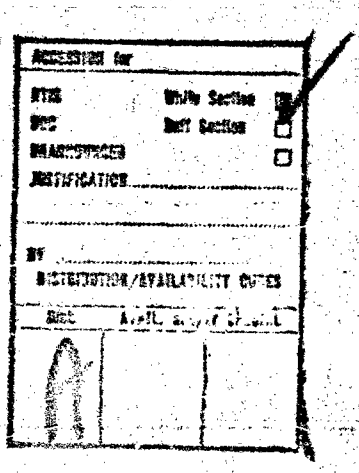

PREFACE

This is one of a series of Aeromedical Reviews entitled "Selected Topics in Laboratory Animal Medicine." These publications contain information on the care and use of animals in biomedical research; they are intended for veterinary educators, managers of animal colonies, and individuals who use animals in scientific investigations. The information in these reviews was initially presented as lectures and handouts in the Laboratory Animal Medicine Residency, the Veterinary Surgery Residency, and the annual symposia on Current Trends in Laboratory Animal Medicine. The authors are veterinarians who are specialists in the respective fields of laboratory animal medicine, pathology, toxicology, and surgery. With few exceptions, the authors are graduates of the Laboratory Animal Medicine Residency conducted at the USAF School of Aerospace Medicine and are certified by specialty boards in their chosen field.

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SELECTED TOPICS IN LABORATORY ANIMAL MEDICINE

VOLUME XXII

THE GUINEA PIG

INTRODUCTION

The purpose of this volume is to bring together pertinent and useful information on guinea pig health, husbandry, physiology, and uses in biomedical research. It is not intended to be a complete bibliography on the guinea pig. The following sections will provide an overall view of the animal's taxonomy, anatomy, physiology, and diseases and supply the reader with information on uses of the guinea pig in research and its potential.

Taxonomic Classification

The guinea pig, Cavia porcellus, is the domesticated member of the genus Cavia. The following is a brief taxonomic scheme with some pertinent comments:

Kingdom - Animal

Phylum - Chordata

Subphylum - Vertebrata

Class - Mammalia

Subclass - Eutheria: These are the placental mammals as compared with marsupials (Metatheria) and egg layers (Prototheria).

Order - Rodentia

Suborder - Hystricomorpha: Animals in this group are said to have "porcupine" form as compared to squirrel-like form (Scuimorpha) or rat-like form (Myomorpha). This group possesses the simple dental formula $\frac{(1\ 0\ 1\ 3)}{2\ (\overline{1}\ \overline{0}\ \overline{1}\ \overline{3})} = 20$.

The infraorbital foramen is large and the masseter muscle insertion passes through the foramen.

Family - Caviidae: The members of this family have four digits on the forefoot and three on the hindfoot. They possess one pair of mammae.

The guinea pig is often called a cavy, this being derived from the genus name. The origin of the cavy is not completely clear but a wild species, Cavia cutleri, was found as a domesticated animal in the homes of Andean Indians when Spanish invaders went into Peru. Shortly thereafter the Dutch imported the animals into Europe and for the next four centuries they were kept primarily as pets by cavy fanciers.

Domestication and Breed Development

Although there are about 20 wild species in the genus (99), only C. porcellus has been domesticated. Guinea pigs are typed according to the length, direction, and texture of their fur. The English type has short smooth hair; the Abyssinian type has short coarse hair that radiates from multiple centers on the body to form rosettes; and the Peruvian type has long (up to 6 inches (15.24 cm)), silky hair (40, 76, 104).

The English type is the one most commonly employed for biomedical research. The animal's color can be albino, white, black, agouti, or sandy. Bicolored and tricolored animals are also found with color distribution usually similar to rabbits (104).

Many strains have been developed in the last 50 years and interested individuals are referred to the most recent printing of the National Research Council - ILAR publication of "Animals for Research" which lists strains and stocks and their availability. The eighth edition (1971) lists four pages of outbred stocks and inbred strains, their origin, where they are maintained, and the type breeding system used (62).

BIOMEDICAL USES

The guinea pig has a wide spectrum of uses in biomedical research. Altnough it does not approach the numbers of rats and mice used, the cavy plays a prominent role; for example, in 1971 there were 646,322 guinea pigs used for research (63).

Immunological Research

Many guinea pigs are used for studies in immunology (10, 12, 14, 40, 76). Guinea pigs are used for the production of complement which in turn is used for a multitude of other immunological tests and investigations. Directly, they are used in studies on anaphylaxis and other allergic manifestations. Catty (12) used the guinea pig to study the immunology of trichinosis. He found that resistance was dose-dependent, long-lasting, and acquired only by infection. His evidence indicated a strong anaphylactic involvement in the immune mechanism. A long-term, sensitizing antibody with biological and physiochemical properties analogous to reagin of humans was demonstrated in the serum of animals infected with the parasite but not in those immunized with worm extracts. Sensitized guinea pig uterus is frequently used to measure reaction to foreign protein by smooth muscle contraction due to histamine release. This is the Schultz-Dale technique. Guinea pigs are particularly useful where information is needed on delayed contact sensitization. Briccetti et al. (10) and Cohen and Sherahama (14) have used guinea pigs in studying both spontaneous and induced amyloidosis.

Nutritional Research

The guinea pig is frequently used in nutritional research. Before the advent of chemical analysis for vitamin C, the guinea pig was one of the major tools in research in that area. They are extremely sensitive to low levels of vitamin C and when used as a bioassay tool they can show deficiency symptoms in 14 to 18 days (40, 76). Additionally, unusually high dietary requirements for folic acid, thiamine, arginine, and potassium have prompted their use in these areas of investigation.

Behavioral and Hearing Research

Based on their behavior, this animal should not be selected for research involving the use of high-frequency noises or electrical shocks because of their tendency to become momentarily immobile or "frozen" when these stimuli are given.

The guinea pig has been used extensively for ear and hearing research. Much work has been done utilizing the cochlea of the inner ear (23, 79, 93, 94) and the external ear as an experimental model for studies of otitis externa

in humans. The clinical appearance of the diseased canal is very similar to that in man (105).

Anatomical Research

An added benefit for many types of studies is to have an animal that delivers such precocious young. The young are more completely developed than any other commonly used laboratory animal (76), and they may be weaned as early as 4 or 5 days of age. Oberg (68) stated that the mandibular joint can be the seat of most pathological conditions seen in articulations in general and that the guinea pig mandibular joint was anatomically larger, histologically more differentiated, and more accessible than those of the mouse, rat, and hamster.

Shively's studies (85) or the systemic arterial pattern of the guinea pig showed a number of deviations from the normal mammalian pattern that could be useful in research on those areas: a) the origin of the vertebral artery has two rami; b) there is a large dorsoscapular artery as a fifth branch of the subclavian artery; c) the bronchoesophageal artery arises from the right internal thoracic artery or the costocervical trunk instead of from the aorta; d) there is a celiomesenteric trunk instead of separate celiac and cranial mesenteric arteries; and e) the renal arteries frequently have a double origin.

Disease Research

The guinea pig is very susceptible to mycobacterium tuberculosis, both the human and bovine strains. The course of infection generally resembles that of a primary progressive infection in man although the rapidity with which characteristic lesions develop may vary with the strain used. It is the chief animal used for the study of brucellosis, diptheria, glanders, endemic typhus, and Rocky Mountain spotted fever. Reid (76) lists many additional diseases for which the guinea pig is a useful research tool.

The guinea pig may be used as a diagnostic tool in differentiating Listeria monocytogenes from Erysipelothrix insidiosa. Inoculation of guinea pigs with L. monocytogenes results in death of the animal whereas E. insidiosa does not kill.

Since the finding of a leukemia virus in the guinea pig by Opler in 1967 (69), interest has been revived in the use of guinea pigs for cancer research. Opler's studies indicated

a remarkable similarity in the evolution of the acute leukemia in his colony to that observed in humans. The leukemia seen in the guinea pigs is an acute lymphatic leukemia and resembles the striking, rapidly fatal disease of children and young adults (69, 70). Recently much research has been conducted in the toxicity of aflatoxins. The guinea pig, with the dog and rabbit, has been shown to be almost as susceptible as ducklings to aflatoxin B (103).

BIOLOGICAL DATA

To understand the health, husbandry, and research uses of the guinea pig, it is first necessary to be familiar with, or at least have reference to, a list of "normal" values. These are listed in tabular form in Tables 1 to 4.

TABLE 1. HEMATOLOGIC VALUES OF THE GUINEA PIG[a]

	Mean	Range
Erythrocytes ($x10^6$)	5-7[b]	4.5-7.0
Packed cell volume (%)	42	37-55
Hemoglobin (gm %)	12-14[b]	11.0-16.5
Mean corpuscular volume (μ^3)	77	71-83
Leukocytes ($x10^3$)	7-10[b]	5-19
Neutrophils (%)	42	15-60
Lymphocytes (%)	49	30-75
Eosinophils (%)	4	1-5
Monocytes (%)	4.3	3-12
Basophils (%)	0.7	0-3
Reticulocytes (%)	0.9	0.4-1.8
Platelets ($x10^3$)		525-900
Sedimentation rate (mm/hr)	1.55	1.5-1.7

[a]Compiled from references 1, 19, 39, 40, 41, 76, 84, and 104.

[b]Range of means given by the various investigators.

TABLE 2. SERUM VALUES OF THE GUINEA PIG[a]

	Mean
Glucose (mg%)	95 (Range 60-125)
Total serum protein (gm%)	4.37
Albumin (gm%)	3.03
Globulin (gm%)	1.34
A/G ratio	2.36:1
Potassium (mEq/liter serum)	6.5
Calcium (mEq/liter serum)	4.8

[a]Compiled from references 1, 19, 39, 40, 41, 76, 84, and 104.

TABLE 3. CARDIOVASCULAR AND RESPIRATORY PARAMETERS OF THE GUINEA PIG

Measurement	Range of values	Reference
Pulse (per min)	130-190	86 and 104
	260-400	90 and 19
Respirations (per min)	100-150	85 and 104
	69-104	90
	90	27
Tidal volume (ml)	1.8	90
Minute volume (liters)	0.16	90
Mean blood pressure (mmHg)	81-90	90
Systolic/diastolic pressure (mmHg)	91/57	59
Blood volume (% body wt.)	4.5-8.3	84
Plasma volume (% body wt.)	3.1-3.8	50
Body temperature (°F)	101-104	18, 85, and
(°C)	38-40	104

TABLE 4. BREEDING AND MATURATION INFORMATION - GUINEA PIG.

	Value
Birth wt (gm)	80 (61-114) (males slightly heavier; smaller litters slightly heavier)
Weaning wt (gm)	180
Weaning age (days)	14-28
Puberty (days)	
Female	28-35
Male	56-70
Breeding age (mos)	3-5
Breeding wt (gm)	
Female	500
Male	550
Litter size	1-6 (avg 3)
Breeding life max (yr)	5
Life-span-max (yr)	8
Estrus cycle (days)	12-18 polyestrous
Estrus period (hr)	7-8 if not mated; 3-4 if mated
Ovulation	Spontaneous
Vaginal plug (hrs)	present 24-48 hrs
Gestation (days)	59-72 (avg 63)

The guinea pig develops an unusual feature in some mononuclear leukocytes--Kurloff bodies. There is some discussion over the composition and function of these bodies, but they are presently thought to be a mucoprotein-mucupolysaccharide complex. Their formative process is felt to be either one of intracellular secretion or of a sequestering and concentration of a serum molecular component (5). They are found as periodic acid-Schiff (PAS) positive intracytoplasmic inclusions which may exceed the size of the nucleus of the cell in which it is found. High numbers may sometimes be found in the red pulp of the spleen, and they can be found in many other organs where they are confined mostly to the vascular channels. They may have a secretory function and be related to estrogen levels and pregnancy. Neonates possess low numbers of these bodies, whereas high estrogen levels and pregnancy stimulated high numbers. Higher concentrations of these bodies may be found in the placental areas.

HUSBANDRY

The principles used in the care and management of guinea pigs closely follow those for the rat, mouse, and hamster. Today most guinea pigs are housed in batteries of plastic, galvanized metal, or stainless steel cages (40, 101). The cages may be either solid bin type or wire-floored varieties, the former being the most common. If wire mesh or expanded metal bottoms are used, the hole size should not exceed 1-1/2" x 1/2" (3.81 cm x 1.27 cm) nor be less than 1/2" x 1/2" (1.27 cm x 1.27 cm) according to NAS-NRC-ILAR recommendations (65). However, some feel that the animals do equally well with 3" x 1/2" (7.62 cm x 1.27 cm) mesh (73). A few facilities use a pen system where the animals are kept in floor pens or tiered pens with bedding provided. This is at best very inefficient utilization of space. Although it is possible to breed and raise litters on wire-bottomed cages, the solid bin type is preferable if proper bedding is supplied to lower the incidence of foot infections, pneumonitis, and "barbering" or chewing of hair.

The current recommendations on space allowances per animal are summarized in Table 5 (65).

Bedding materials, if used, are a potential source of several problems. Infectious agents may be present in vermin-contaminated bedding. Coarse bedding may affect reproductive performance by lodging in the vulva and providing penile irritation to the male during copulation. Fine bedding may produce inhalation or sensitization problems.

TABLE 5. RECOMMENDED CAGE SPACE ALLOWANCES FOR THE GUINEA PIG

	Sq. in. (sq. cm) per animal	Height
Up to 250 gm	43 (277)	7 (15.2)
250-350 gm	58 (374)	7 (15.2)
Over 350 gm	101 (652)	7 (15.2)

The guinea pig is probably more sensitive to variations in temperature and drafts than any of the other common laboratory animals (73). Although there are minor differences in published values, the optimum range of temperature is 55° to 75°F (13° to 24°C); and the relative humidity should be 40% to 60% (65, 73, 75, 86, 101, 104). Control of temperature fluctuation and drafts is more important than the actual temperature.

Guinea pigs do not do well when they are moved or disturbed frequently. Moving and handling guinea pigs have resulted in large weight losses within 24 to 48 hours. This weight is regained rapidly if the conditions are stabilized, but interpretation of experimental data could still be confused.

Breeding systems vary and no one system is best. Each system has certain advantages and disadvantages which must be considered in arriving at an optimum system for a particular need.

The simplest system is monogamous pairs but requires too many males to be maintained for most breeding colony operations (104). An advantage of the system is the high percentage of postpartum matings.

A nonintensive method has been used that allows a variable number of sows kept as a harem with one boar. Some breeders recommend 5 to 10 sows per boar (104), but 4 to 5 is probably preferable. Females are removed in late pregnancy and allowed to farrow individually and raise the young to weaning age before being returned to the harem. About 12 young per sow per year can be expected with this system. Accurate record keeping is still possible, and the groups are small enough that infectious diseases can usually be controlled.

A communal farrowing system can be used in which heavily pregnant sows are removed and allowed to farrow and raise their litters together (75, 104). This method is quite common.

Polygamous groups, where the sows and boars remain together as a static colony and the young are reared communally, produce 14 to 16 young per year per female (104), but 12 per year is average. Record keeping becomes more difficult with this method; there is a higher number of newborn fatalities, but this is offset by an increase in postpartum matings. With the latter two systems a problem sometimes arises when the eldest litter strips the milk from all the nursing sows in the pen (75).

NUTRITION

Nutrition of guinea pigs is a difficult topic to discuss briefly--not that so much is known but because so little is known. Most of the "requirements" found in the literature are not "minimum daily requirements" but would more properly be called "adequate nutritional levels" that were derived from food analyses of existing diets that are nutritionally adequate.

The adult guinea pig weighs from 700 to 1600 gm, depending on age and sex, and females are smaller than males (74, 76). They eat up to 1/12 of their body weight in food per day and the water requirement is about 50 to 100 ml per day.

The values listed below are acceptable levels of ingredients that meet the known dietary requirement of growing guinea pigs (40, 64, 66, 76).

Ingredient	Amount*
Total food (gm)	80
Total protein (% of diet)	20
Fat (% of diet)	3
Carbohydrate (% of diet)	45
Calcium (gm)	1
Phosphorous (gm)	.5
Magnesium (gm)	.28
Potassium (gm)	1.12
Cobalt (µg)	2
B-Carotene (gm)	9.6
α-Tocopherol (mg)	4.8
Vitamin K (mg)	.8
Ascorbic acid (mg)	16
Thiamine (mg)	1.3
Riboflavin (mg)	1.3
Vitamin B_6 (mg)	1.3
Niacin (mg)	4
Pantothenic acid (mg)	1.6
Folic acid (mg)	.8
Choline (gm)	.12
Vitamin B_{12}	Not required if adequate cobalt is in diet

*These values are based on a kilogram of body weight unless otherwise indicated.

The guinea pig, like man and other primates, needs ascorbic acid (vitamin C) in the diet. Sixteen mg/kg body weight is sufficient to prevent all disturbances in a scorbutic animal. Although this requirement can be met by supplying fresh green vegetables, it is a more common practice to feed a commercially prepared guinea pig diet containing adequate ascorbic acid. This method eliminates the hazard of diarrhea and infection which appear to have a higher incidence in cages containing moist wilted vegetable material (22). If commercial diets are the sole nutrient source, it is recommended to order the food at least monthly and store it in a cool environment. Most animal-holding facilities in the United States compromise and feed a vitamin C-fortified pelleted chow with a minimal supplementation of fresh lettuce or other green vegetable.

BACTERIAL DISEASES

Salmonellosis (Paratyphoid)

Salmonellosis is probably the most lethal disease of guinea pigs (81, 104). Several members of the genus Salmonella--including S. dublin, S. limetes, and S. enteriditis--have been isolated from cases of salmonellosis in guinea pigs, but S. typhimurium is the most common (49, 75, 81, 104). Since wild rodents are a likely source of these organisms, it is extremely important to take precautions to avoid vermin contamination of the feed and bedding.

Clinically, the disease may be peracute, acute, or chronic. In the peracute or acute form, mortality may approach 90% to 100% (49, 73). Initially, only one or two deaths may be noted followed by a 2- to 3-day lull. Disaster within a colony may be averted if a clinician isolates Salmonella sp. at this time and destroys all guinea pig contacts. After the 2- to 3-day lull there is a rapid rise in fatalities for a few days. After 10 to 15 days a more chronic form of the disease appears with more clinical signs and more necropsy lesions but a lower mortality. Animals necropsied after peracute death may show no signs of the disease other than an enlarged spleen. Animals dying from the acute form may have nonelevated small foci of necrosis in the liver and spleen. Enlarged lymph nodes may also be present. As the disease becomes more chronic the degree of necrosis continues until hepatic and splenic abscesses become evident (49, 73, 104). The intestine becomes progressively involved in chronic cases. Animals which recover from the disease may become carriers and are capable of spreading infection to nonimmune guinea pigs brought into the colony.

Treatment is not generally attempted; healthy animals are usually isolated while infected ones are destroyed. A bacterin of S. typhimurium with incomplete Freund's adjuvant was employed (36) and produced significant serum agglutination titers in guinea pigs. This could be valuable in controlling an outbreak of salmonellosis due to S. typhimurium in a colony.

Pseudotuberculosis

Pseudotuberculosis in guinea pigs is caused by Yersinia pseudotuberculosis. The route of infection, as with salmonellosis, is usually by ingestion of contaminated food or water. Acute or chronic forms of the disease may occur with the latter being most common. The acute disease presents a typical picture of acute septicemia and probably results from rupture of an abscessed mesenteric lymph node into venous or lymphatic circulations. Miliary lesions may be found in the liver and lungs in these cases (73, 104).

Usually the disease is chronic and starts with lesions in the Peyer's patches of the small intestine (81, 104) and progresses to the primary site of involvement, the mesenteric lymph nodes (73). The organism produces necrotic foci that enlarge to form caseous nodules in affected lymph glands, spleen, or liver; and unlike the lesions produced by Salmonella, the lesions bulge above the surface of the gland or organ. This chronic form may cause progressive emaciation and death over a 3- to 4-week period. Paterson (73) stated that the mesenteric gland is the site of the primary lesion in 99% of naturally acquired infections and that affected animals can be easily culled by manually palpating early lesions. A less common nonfatal form of the disease starts and localizes in the lymph nodes of the head and neck. Rupture of these lesions can lead to rapid spread within the colony.

A combination of good sanitation, palpation, and culturing of the organism from new additions to a colony and elimination of positive animals should control pseudotuberculosis in guinea pigs.

Cervical Adenitis and Lymphadenitis

Infections of Streptobacillus moniliformis in guinea pigs cause formation of abscesses that may become large in the regional lymph nodes. Usually no signs of pain or systemic effects are noted (104). The disease is usually associated with the feeding of coarse hay or other food capable of abrading the buccal mucosa (49, 73, 104).

In addition to Streptobacillus moniliformis, Yersinia pseudotuberculosis can be localized in the lymph nodes of the neck and head, and there are a number of other organisms that may produce similar signs. Streptococcus pyogenes, S. zooepidemicus (49, 81), Actinomyces muris (49), Bacteriodes caviae (49), Salmonella limete (104), and the fungus Mucor (81) have all been implicated. S. pyogenes can also produce septicemia, pneumonia, and purulent arthritis. Although treatment may not always be indicated, the condition has been successfully treated using 12.5 mg of Cephaloridine once a day in the water for two weeks (17).

Miscellaneous Streptococcal Infections

Gupta et al. (32) isolated an alpha hemolytic streptococcus from two guinea pigs with mastitis and high leukocyte counts in their milk. A similar organism along with Micrococcus sp. and Enterococcus sp. was found in various milk samples in another test (33). In the latter study a total of 51% of the milk samples from multiparous guinea pigs cultured during the first two weeks of gestation were positive.

Tuberculosis

The guinea pig is susceptible to both human and bovine strains of Mycobacterium tuberculosis by natural infection (49). It is a highly fatal disease but fortunately its occurrence is rare (49). The liver and spleen are the most severely involved organs and the lungs are involved to a lesser degree (81).

Botryomycosis

This bacterial disease is characterized by a mixed granulomatous and suppurative inflammatory reaction in which the diagnostic feature is the presence of fungus-like granules (49, 81). Bostrom et al. (9) described two cases in which

guinea pigs had severe focal necrotizing pneumonia caused by Pseudomonas aeruginosa. Numerous "sulfur granules" containing the organisms could be found in the pneumonia areas (81). Pseudomonas aeruginosa infection additionally may cause subcutaneous abscesses, draining lymph nodes, conjunctivitis, and ophthalmitis (49). Transmission is usually by direct contact or contaminated drinking water.

Pneumonia

Bacterial pneumonia in guinea pigs is caused by a wide range of organisms. Some have been alluded to already: M. tuberculosis, S. pyogenes, and Ps. aeruginosa. Diplococcus (Streptococcus) pneumoniae, Klebsiella pneumoniae, Pseudomonas caviae, and Bordetella bronchiseptica can all be added to the list. Regardless of the organism the symptoms are similar: nasal discharge, sneezing, rales, and dyspnea. Although these organisms are endemic in many stocks, losses from pneumonia may only be sporadic and confined to adult breeding stock; but epidemics may occur in young stock subjected to stress (49, 73). Pneumonia should not be a serious problem in a well-managed colony.

In many species B. bronchiseptica is merely a causal finding, but Nakagwa et al. (61) established it as a primary pathogen in guinea pigs by experimental transmission, detailed studies of the disease progression in experimentally infected animals, and by monitoring serum agglutination titers. Nikkels and Mullink (67) have controlled two outbreaks of this infection in an SPF breeding colony by using an autovaccine in the breeding animals.

Miscellaneous Bacterial Infections

Coagulase positive Staphylococcus aureus organisms can cause subcutaneous abscesses, chronic pododermatitis (91), and uterine infections (46).

Schiff et al. (83) recently reported on enteropathogenic Escherichia coli in laboratory animals and mentioned that enteropathogenic E. coli cause gastroenteritis in human infants and in laboratory animals. Since a high percentage of guinea pig populations harbor the organisms asymptomatically, they may provide a source for future epizootics.

VIRAL, MYCOPLASMAL, AND CHLAMYDIAL INFECTIONS

Viral Infections

Viral infections in the guinea pig are uncommon when compared with most of the other species of laboratory animals and may be partially due to the minimal exposure that the guinea pig has had to virologic research. As investigators begin to use more sophisticated techniques and actually search for viruses, perhaps more viral agents will be recovered from guinea pigs. Although clinical disease in guinea pigs caused by viral agents is uncommon, latent infections may be present that interfere with research manipulations or the interpretation of data.

Herpes-Like Virus

An indication of this situation is the identification in 1969 of a herpes-like virus in guinea pigs (GPHLV) by Hsiung and Kaplow (44). Subsequent studies demonstrated in a survey of over 200 guinea pigs from five strains that over 90% of Strain 2 and 35% of Muta strain guinea pigs showed herpes-like virus infection (43). The virus was widely distributed in the various tissues and organs as well as in white blood cells and persisted for as long as 10 months without any evidence of clinical disease. Transmission of the agent across the placenta was established by Lam and Hsiung (52), and they postulated a hematogenous dissemination in which the virus-carrying white blood cells played an important role. No histopathologic changes or inclusion bodies were found in either the maternal or fetal tissues. In another study of the same agent (8) the virus was recovered 7 to 8 months after being experimentally injected intracerebrally into guinea pigs and mice. A few cells with inclusions were found. Bhatt et al. (6) isolated a herpes-like virus from apparently healthy, naturally infected Strain 2, Strain 13, and Hartley Strain guinea pigs that was antigenically similar to the virus of Hsiung but different from guinea pig cytomegalovirus.

Salivary Gland Virus

Salivary gland virus infection is common and usually caused by a latent infection of cytomegalovirus, another virus of the herpesvirus group. Surveys estimate that the incidence is 70% to 80% (49, 81). The virus nature of the highly host-specific cytomegaloviruses which infect many species was first established in guinea pigs, and the guinea pig remains the

favorite laboratory animal model for researchers studying this disease (81). The disease is usually recognized by finding large eosinophilic or basophilic inclusion bodies in the nuclei of the ductal epithelium of salivary glands (88). Small intracytoplasmic inclusions were also observed (49, 81). Serial passage of this agent through young guinea pigs enhances its virulence until it may kill susceptible animals in 6 to 26 days (49). Intracerebral inoculation produces irritability, ataxia, tremors, convulsions, and death within 6 days.

Guinea Pig Paralysis

Guinea pig paralysis (49, 73, 104) is a noncontagious sporadic disease that occurred in a laboratory colony in Germany in the early part of this century. A filtrable agent was recovered that caused a nonsuppurative cerebrospinal leptomeningitis and lymphocytic infiltrations in the gray matter of the spinal cord, especially in the lumbar region. The clinical course started with urinary incontinence and hindleg weakness which progressed to paralysis and death in 8 to 10 days. No cases have been reported since the original outbreak.

Lymphocytic Choriomeningitis

Lymphocytic choriomeningitis is an acute infection of the LCM virus in guinea pigs but it is usually a mild infection. Fatalities due to a paralyzing lymphocytic meningoencephalitis have been described; however, the usual lesions are limited to a perivascular lymphocytic cuffing about small vessels of the brain, liver, kidneys, and other organs (49).

Leukemia

Cavian leukemia is an acute virally induced fatal lymphoblastic leukemia in which death ensues about 5 days after initial appearance of lymphoblasts in the peripheral blood (81). This disease closely resembles the acute, fulminating leukemia found in infants and young adult humans (69, 70). At necropsy the peripheral and visceral lymph nodes, spleen, and liver are markedly enlarged; and there is a generalized infiltration of all tissues by the leukemic cells and normal architecture may be lost. Infarction of the spleen and kidney and necrosis of affected lymph nodes have been reported (81). These findings parallel those found by Ediger and Rabstein (20) who described a similar picture in the one

case they found in over 15,000 necropsies over a 16-year period.

Anderson and Jeppesen (2) have described virus-like particles in oogonia and oocytes of fetal, neonatal, and adult albino guinea pigs by electron microscopy. The particles were identical to the guinea pig leukemia virus in morphology and intracisternal cytoplasmic location. Attempts to culture the virus on tissue culture were not successful.

Mycoplasmal Infections

Mycoplasma infections are not considered of clinical importance in guinea pigs. This statement may not be appropriate in the future identification as isolation techniques improve. Hill et al. (37) isolated mycoplasma organisms from guinea pig nasopharynx, brain, and genital tracts that were not M. pulmonis, the mycoplasma responsible for infectious catarrh in mice. The case in which the isolation was made from the genital tract was from an animal that died with metritis and no other pathogens could be found. The same author (38) made seven isolations from guinea pigs, one of which had metritis. All seven were different from known mycoplasma based on serology and biochemical reactions and he proposed the name M. caviai.

Chlamydial Infections

This group of organisms which has had other names--Miyagawanella, Bedsonia--is not of clinical importance, but members of this group have been found in guinea pigs. Robinson (80) recovered these organisms by serial blind passage in chick embryo yolk sacs from 4 of 15 guinea pigs housed in a conventional colony. The interesting aspect (and the only reason for mentioning it) was that direct ancestors of these guinea pigs had grazed on grass paddocks that had contained lambs discharging the organisms of enzootic abortion (Chlamydia ovia) 15 years previously. It is fascinating to envision the possibility that this agent could be vertically transmitted over that long period.

PARASITIC AND FUNGAL DISEASES

Internal parasites of clinical importance in the guinea pig are few, but it is important to be aware of the varicus species which can be found.

Protozoan Diseases

Intestinal Coccidiosis--This is a fairly common disease in guinea pigs. For practical purposes, coccidiosis in guinea pigs refers to infection with the intestinal protozoan Eimeria caviae (81, 104). Infection occurs in the superficial epithelium of the large intestine. The colon becomes distended with gas and the wall becomes dark red and may be petechiated. Whitish-gray nodules which represent the mature schizonts may be visible in the mucosa (81). Pathogenicity is only moderate and deaths are rare with coccidiosis. Affected animals exhibit diarrhea, anorexia, and lethargy. Diagnosis is made by demonstrating oocytes in the feces. Since the oocytes require at least 6 days to become infective, control is based on regular cage cleaning (104).

Renal Coccidiosis--This is a rather rare, benign disease caused by Klossiella cobayae, a member of the order, Coccidia. Although these organisms reside in and destroy some of the epithelial cells of the convoluted tubules, they are usually an incidental histologic finding. Complications in interpreting experimental data can occur since Hofmann and Hanichen (42) reported irregular lymphocytic and histocytic invasion of the interstitium and frequently a fibroblast multiplication in the interstitial tissue of the corticocapsular border. The same authors found the organism in 31 of 108 clinically normal guinea pigs indicating that, once established, significant numbers of animals may be infected.

Toxoplasmosis--Another coccidial organism, T. gondii, has rarely infected guinea pigs. The organisms are about 2 x 4 microns and can be found free in the tissue or within cysts. Infection induces a granulomatous response in many organs, including the brain, liver, lungs, and lymph nodes which are particularly involved. Kunz and Hutton (49) describe a condition of latency which, upon stress, becomes an acute syndrome with spastic paralysis followed by death in 6 to 7 days. Diagnosis is usually based on demonstration of the organisms which are gram-negative and strongly PAS positive.

Nosematosis--Encephalitozoon cuniculi is smaller than T. gondii (0.8 x 2 microns), gram-positive, and only weakly PAS positive. Focal granulomatous nephritis and myocarditis lesions have been described but the disease is mild and not overt.

Cryptosporidiosis--There are about six species of the genus Cryptosporidium. Although there is confusion and debate

on the proper species names, Vetterling et al. (96) appear to have justified C. wrairi as the agent infecting the guinea pig. This intestinal coccidian may cause a chronic enteritis with no overt clinical disease (81, 96). The organisms are found in the microvilli on the small intestine epithelium and are 1 to 4 micron, round bodies. The organism, unlike E. caviae, does not invade the cell.

Other Intestinal Protozoans--A number of parasitic flagellates have been reported from guinea pigs that are of questionable pathogenicity importance: Hexamastia caviae, H. robustus, Proteromonas brevifilia, and Caviamonas mobles. These infest the guinea pig cecum. Other nonpathogenic parasites found in the guinea pig cecum are: Chilomastix intestinalis, C. wenrichi, Selenomonas palpitans, and a species of Monocercomonoides (29).

Metazoan Parasites

Probably the only important helminth parasite of guinea pigs is Paraspidodera uncinata. These nematodes of the ascarid family are about 11 to 37 cm long, and, unlike most ascarids, reside in the cecum. Although they may be present in large numbers, they usually do not produce significant lesions (29). The life cycle is direct and the prepatent period is 37 to 64 days and the patent period 12 to 39 days (54). Ascarid-type eggs can be detected in the feces and average 43 x 31 microns (54).

Fasciola hepatica infestation with the parasite found in the liver and muscles has been reported as has infestation by Trichinella spiralis. Neither are considered important to the animal's health.

External Parasites

Lice--Several species of lice may infest the guinea pig and they are all classified as biting lice:

1. Gyropus ovalis
2. Gliricola porcelli
3. Tremenopan jenningsi, T. hispidum
4. Menopon extranium

The first two are most common and often occur together. These lice live on skin debris, and a light infestation may cause no signs; however, a heavy infestation leads to scratching and self-mutilation (29). The parasites (and lesions)

tend to be concentrated about the head and ears (49, 73). Standard procedures of dusting or dipping may control the infestation, but complete elimination of the parasites from the colony is difficult.

Mites--Chirodiscoides caviae infestations appear to be more common than the literature reports would indicate, at least in certain geographical areas (98). Heavy infestations may cause alopecia and severe irritation (29), although other heavy infestations--up to 200 mites/sq cm--caused minimal adverse effects (98).

Fungal Infections

Phycomycosis (Mucormycosis)--Infection with various members of the class Phycomycetes can cause a granulomatous reaction. Absydia corymbifera or A. ramosa are two of the more common agents isolated. The organisms usually are ingested on moldy feed and localized in the mesenteric lymph nodes (104). These nodes form a benign mass in the abdomen that frequently is palpable (similar to pseudotuberculosis). According to some authorities, but disputed by others, the mass attains maximum size in 14 to 21 days then gradually recedes (49). In contrast to pseudotuberculosis in which the lymph nodes do not recede, the course is usually one of diarrhea, progressive emaciation, and death. Occasional fatalities may occur if infection spreads to the liver, spleen, or kidneys (49, 81, 104). Microscopically the lesions consist of multiple granulomatous foci, some with central coagulation necrosis, composed of fibroblasts, histocytes, lymphocytes, plasma cells, and occasional multinucleated giant cells (81, 88). The organisms may be seen with hematoxylin and eosin, but are more easily demonstrated with the use of Gomori's methenamie silver, or PAS strains as nonseptate, irregularly branching, coarse hyphae (81, 88).

Dermatomycosis (Ringworm)--Infections that may approach epizootic proportions in guinea pigs have been caused by Trichophyton mentagrophytes. The lesions, which usually start about the nose, are superficial in nature and can be diagnosed by microscopic examination of appropriately cleared skin scrapings (88).

MISCELLANEOUS CONDITIONS

Pregnancy Toxemia

Pregnancy toxemia is a sporadic disease usually associated with well-nourished sows in late pregnancy but can also affect virgin guinea pigs. The disease has an acute onset with the earliest signs being anorexia, adipsia, dyspnea, and agitation (26, 81). Marked weight loss may occur. The urine of the guinea pig (usually pH 9) becomes acid (pH 5 to 6) and contains variable amounts of protein and ketones. The disease progresses to coma and death in 4 to 5 days unless interrupted by parturition (26). Death can occur in as little as 24 hours, however (104). The primary lesion seen at necropsy is a diffusely fatty liver (81). Although endocrine imbalance may clearly be a factor (81), the obesity of the animal, its prior and present nutritional state, and the existence of stress all seem interrelated in the pathogenesis of the condition.

Metastatic Mineralization

This condition is common in guinea pigs over one year of age (49). The cause is presumed to be a dietary Ca:P imbalance or a magnesium deficiency (38), but Sparschu and Christie (89) found extensive deposits of calcium in the trachea, lung, heart, colon, liver, stomach, and kidneys in 9% of 140 2-year-old guinea pigs whose diets contained 1.33% Ca, 0.87% P, and 0.27% Mg. Kaufmann (48) states that the condition is probably one of an osseous metaplasia and is not due to inhalation of fish bone of dietary origin as has also been incriminated (45). Kaufmann studied guinea pigs which had never received animal protein and therefore had no occasion to inhale an aerosol which may have contained bone particles.

Rhabdomyomatosis

Rhabdomyomatosis is an incidental lesion found at necropsy in guinea pigs and is characterized by the presence of large vacuolated myocardial muscle cells (81). The vacuoles contain a highly soluble glycogen and this lesion is thought to represent a disturbance in glycogen metabolism (49). Most of the lesions are found in the left ventricle, beneath the endocardium, epicardium, or in the myocardium (97). The incidence may range up to 12% in some colonies (49).

Perivascular Lymph Nodules

Perivascular lymph nodules in the lungs are frequently seen in guinea pigs (81, 92), usually in older animals but have been found in animals only 5 days old. Although most often microscopic in size, the nodules may reach 0.5 mm in diameter and may be grossly visible as white foci (81). Microscopically the nodules consist of accumulations of lymphocytes adjacent to, or surrounding, blood vessels and occasionally bronchioles. Germinal centers have been observed in some of the larger nodules. The cause is unknown but the researcher should be aware of their possible existence.

Osteoarthritis

Osteoarthritis has been reported in guinea pigs (34). The front feet are more frequently involved and the conditions appear to have predisposing factors of senility and trauma. Staphylococcus aureus is frequently isolated from these lesions. Pododermatitis caused by the same agent has also been reported (91).

Congenital Abnormalities

Although few in number, congenital abnormalities have been reported. Scleral dermoid (31), conjoined twins (47), and absence of a uterine horn (7) have been reported.

Scurvy (Vitamin C Deficiency)

The guinea pig can become scorbutic on a vitamin C-deficient diet in three weeks. Vitamin C is needed for normal metabolism of tyrosine (51), phenylalanine, dehydrophenylalanine, and for the oxidation of tryptophan to 5-hydroxytryptophan (15, 77). The most important role of vitamin C is in the formation of mesenchymal tissue derivatives and is needed for the production of dentine (16, 25), osteoid, collagen (78), and intercellular cement substance. For this reason maintenance of vascular integrity is also an important function of vitamin C.

The lesions resulting from this altered metabolism are: failure of formation of an osteoid matrix in bone, loose periosteum, subperiosteal hematomas, microfractures, poor wound healing, loosening of teeth, hemorrhages, and production of a normochromic, normocytic anemia (77).

As discussed in the section on nutrition the best treatment is prevention by feeding an adequate diet.

PHARMACOLOGY

Antibiotic Therapy

Antibiotics should not be administered to guinea pigs without close scrutiny of the drug, dose, and route selected. Deaths that frequently follow antibiotic administration are currently believed to be not due to the sensitivity of the animal itself but to the sensitivity of the gastrointestinal flora. An enterocolitis and coliform bacteremia are produced, and the flora composition of the intestine changes from one that is primarily gram-positive to one that is primarily gram-negative (49). Small (87) gave guinea pigs a variety of antibiotics by oral and parenteral routes and found that the same effect (fatal enterocolitis) was produced. Fortifying this "altered flora" theory is evidence that lethal effects of penicillin G given intraperitoneally were absent in germ-free guinea pigs but caused 50% mortality in guinea pigs from conventional colonies. The following are examples of antibiotic administration resulting in guinea pig deaths:

1. Aureomycin hydrochloride, 10 mg/kg given subcutaneously, is lethal in 4 days.

2. Crystalline sodium penicillin G, 10,000 units kg/d subcutaneously, kills the animals in 3 days.

3. Bacitracin, 1,000 units per os, is 100% fatal.

4. Erythromycin, 33 mg/kg, intraperitoneally for 3 days, is 100% fatal.

5. Chlortetracycline, 20 mg/os, is fatal.

Chloramphenicol, however, given per os at 40 mg/d for 6 days, was <u>not</u> fatal or toxic.

Anesthetics, Tranquilizers, and Disassociative Drugs

Thiobarbiturates and oxybarbiturates are commonly used for guinea pig anesthesia. The drugs can be given intraperitoneally or intravenously using the ear vein, penile vein, or the saphenous vein, about 1/2" (1.27 cm) above the hock (27).

The animals should be fasted overnight. Pentobarbital sodium is given at 28 mg/kg while thiopental sodium is given at 30 to 45 mg/kg.

Methoxyflurane is the most commonly used inhalant anesthetic and the mortality rate is lower than with the barbiturates. Animals induced with this drug go through a swimming motion just prior to reaching a surgical plane of anesthesia. If needed, animals can be resuscitated by placing the large end of a 10 cc plastic syringe holder over the animal's nose and blowing through the small end which should have a hole cut in it. This mouth-to-mouth method is simple and practical.

Chlorpromazine at 1 to 5 mg/kg provides effective tranquilization. Effective analgesia, sedation, and tranquilization have been obtained using a commercial preparation containing 0.5 mg fentanyl and 20 mg droperidol per ml (Innovar-vet, McNeil Laboratories) (55). The drug is given intramuscularly at a dosage of 0.08 ml to 0.15 ml/kg.

The disassociative drugs, phencyclidine hydrochloride and ketamine hydrochloride, have been successfully used in guinea pigs. Phencyclidine at 1 mg/kg IM produces a quiet, calm animal for about 2 hours; at 3 mg/kg IM it produces a cataleptoid state with some depression and the effects last about 6 hours. Weisbroth and Fudens (100) used ketamine HCl intramuscularly at 44 mg/kg in guinea pigs. These animals lost reaction to painful stimuli for 15 to 25 minutes and they did not resist dorsal recumbency. They found that adjunctive treatment with atropine (0.05 mg/kg) eliminated a tendency for excess salivation.

NEOPLASMS

It is not the intent of this review to delve into the histologic characteristics of the various tumors of the guinea pig but to report on the incidence of tumors so the investigator can be made aware of them.

There are surprisingly few reports of tumors in guinea pigs; however, this may be misleading. Guinea pigs used for research are usually euthanized before they attain an age when one would expect to find a high incidence of tumors. Breeders frequently cull older animals from their breeding stock without a necropsy being performed.

Rogers and Blumenthal (82) reported 14 spontaneous tumors in an inbred strain of guinea pigs over a 10-year period. There were no tumors in any animals under 3 years of age, supporting the belief that only the older stock is at a high risk. The 14 tumors represented an incidence of 14.4% of the animals surviving for over 3 years. The same authors reported no tumors in another strain kept for a like period. Variation between the strains would be important to the investigator in a chronic study; but unfortunately, data for all strains were not available. A summary of the tumors reported on up to that time is presented with comments and references.

Tumors of the respiratory tract appear to be the most common type of growth (24, 82). With few exceptions (28) the tumors are papillary adenomas. Tumors of the reproductive tract are the second most common category. The types are quite varied with the following reported: ovarian teratomas (35, 102), uterine leiomyomas (82), fibromyomas (56), leiomyosarcomas (82), fibrosarcomas (82), myxosarcomas (82), mixed mesenchymal tumors (82), and testicular embryomal carcinomas (82).

In the reticuloendothelial system, splenomas (30), lymphosarcomas (18, 60) and leukemias (13, 20, 57, 69, 70, 81) have been reported. About a dozen tumors of the mammary glands are reported in the older literature (before 1950), and about 75% of these were adenocarcinomas. Tumors have been reported from most of the major organs including: skin (21, 35), eye (11, 31), brain (58), heart (3, 4), gastrointestinal tract (71), kidney (95), endocrine system (71), bone (53, 72), liver (82), and gallbladder (82).

Based on the above information, any person working with guinea pigs should be aware of the possibility of a neoplasm in any of the organs of guinea pigs over 3 years of age.

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